

CLAIMS:

1. A composition for the treatment of a disease involving active angiogenesis which comprises a vascular damaging agent other than a cytokine releasing anticancer agent together with an inhibitor of the formation or action of nitric oxide in a mammalian system.
2. A composition for the damage of the formation of new vasculature by angiogenesis comprising a combination of a vascular damaging agent other than a cytokine releasing anticancer agent and an amount of an inhibitor of nitric oxide synthase in an amount sufficient to augment the effect of the vascular damaging agent.
3. A composition according to claim 2 wherein said vascular damaging agent is selected from a tubulin-binding agent or an antibody targeted to vasculature.
4. A composition according to claims 2 and 3 wherein the nitric oxide synthase inhibitor is selected from a derivative of arginine, ornithine, lysine, citrulline, S-alkylthioureas or aminoguanidine.
5. A composition according to claim 4 wherein the nitric oxide synthase inhibitor is an N^G-substituted L-arginine selected from N^G-nitro-L-arginine and alkyl esters thereof, N^G-methyl-L-arginine and N^G-amino-L-arginine.
6. A composition according to claim 4 wherein the derivative of ornithine is L-N6-(1-iminoethyl)-ornithine.
7. A composition according to claim 4 wherein the derivative of lysine is L-N6-1-iminoethyl)-lysine.
8. A composition according to claim 4 wherein the derivative of citrulline is selected from L-thiocitrulline, L-homothiocitrulline or an S-alkylthiocitrulline particularly S-methyl-L-thiocitrulline.

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Q2 s 9. A composition according to any one of claims 1 to 8 which also comprises a pharmaceutically acceptable excipient appropriate to the method of administration.

10. A composition according to any one of claims 1 to 9 wherein the composition is in the form of a kit, one part of the kit containing the vascular damaging agent and the second part of the kit the nitric oxide inhibitor.

10 11. Use in the preparation of a medicament for the treatment of disease involving active angiogenesis and containing a vascular damaging agent other than a cytokine releasing anticancer agent characterised in that the medicament also contains an amount of an inhibitor of formation or action of nitric oxide sufficient to augment the effect of the vascular damaging agent.

15 12. Use according to claim 11 wherein said inhibitor of formation or action of nitric oxide is a nitric oxide synthase.

20 13. A method of treatment for a mammal having a disease involving active angiogenesis said method comprising administration of a vascular damaging agent other than a cytokine releasing anti cancer agent and an amount of an inhibitor of formation or action of nitric oxide in amount sufficient to augment the effect of the vascular damaging agent.

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25 14. A method according to claim 13 wherein the vascular damaging agent and nitric oxide inhibitor are administered substantially simultaneously but separately to the mammal under treatment.

30 15. Use of inhibitors of nitric oxide formation or action in the preparation of a medicament for augmentation of the effects of a vascular damaging agent other than a cytokine releasing agent.